Attorney Docket No.: 133001.00101

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application No.	:	10/036,066
Applicant	:	Scott L. Diamond
Filed	:	November 7, 2001
Group Art Unit	:	1641
Examiner	:	Ann Y. Lam
Docket No.	:	133001.00101
Confirmation No.	:	3883
Customer No.	:	21269

Title: PEPTIDE OR PROTEIN MICROASSAY METHOD AND APPARATUS

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

DECLARATION UNDER 37 C.F.R. § 1.132

Sir:

I, Scott L. Diamond, declare as follows:

1. I am the named inventor of the invention described and claimed in the above-identified application.

2. I am a citizen of the United States, and reside at 610 Yale Road, Bala Cynwyd, PA 19004, Montgomery County. I graduated from Cornell University in 1986 with a bachelor's degree in chemical engineering and from Rice University in 1990 with a Ph.D. in chemical engineering.

3. From 1990 to 1997, I was a faculty member at the State University of New York. From 1997 to the present, I have been a faculty member of Penn Engineering, where I

hold the Arthur E. Humphrey Chair of Chemical and Biomolecular Engineering and Bioengineering. In addition, I am the Associate Director and Charter Member of The Institute for Medicine and Engineering; Director, Biotechnology Program; and Director, Penn Center for Molecular Discovery.

4. I have read and am thoroughly familiar with the contents of the above-identified patent application.

5. I declare that the claimed invention is directed to an assay system comprising a computer and a set of operating instructions resident in computer software of the computer for operating, a set of reactant dot applicator pins, a separate device for biological sample aerosol mist generation, an xy positioner operatively connected to the dot applicator pins, and a chamber within the device for biological sample aerosol mist generation for control of biological samples, wherein the dots have a diameter ranging from 10 microns to 100 microns and have one or more constituents therein, wherein the aerosolized biological sample mist droplets are applied simultaneously by the separate device for sample aerosol generation without forming a wetting film, for computer-enhanced assay of any reaction between the sample mist droplets and the constituents, and wherein the dots are not covalently bound to a substrate.

6. As an expert in the field of biotechnology, I can attest that never has it been possible before the present invention and, indeed, is extremely difficult, to rapidly and uniformly deliver an aerosolized mist to adherent droplets, each droplet having a diameter ranging between 10 microns and 100 microns and separated only by a center to center distance of only 50 microns to 500 microns, without cross-contaminating the droplets or changing the position of each droplet.

7. Furthermore, the aerosolized biological sample mist of the claimed invention can be deposited in a highly uniform manner without the generation of a continuous wetting film which destroys the positional isolation of each adherent droplet.

8. The claimed invention therefore provides the unexpected finding of the generation of an aerosolized mist that is so fine so as to deposit the aerosolized mist on an array to mix with the adherent droplets while at the same time evaporating very rapidly when the aerosol mist hits the substrate. In this way, each droplet is and remains isolated from every other droplet (See FIGS. 13A-13D; Exhibit A); and each droplet is and remains positionally unperturbed and unmoved (See FIG. 17; Exhibit B)

9. The above-described unexpected phenomenon of the claimed invention is shown with striking clarity in FIG 1.ED; Exhibit C. This figure contains four panels which show the delivery of the aerosolized mist to each droplet, in which the aerosol evaporates between the droplets within 7 seconds while never reaching a percolation limit, thereby preventing cross-contamination of the droplets.

10. Furthermore, the surprising and unexpected reaction isolation between each droplet is shown clearly in FIG.2.ED; Exhibit D. This figure illustrates the aerosol deposition of a mist with a green dye (the paler droplets) on an array containing alternating rows of droplets containing blue dye (the whiter droplets) and rows of droplets lacking dye (the paler droplets). This unexpected reaction isolation between each droplet is maintained indefinitely, whereby the blue dye does not cross-contaminate into the rows lacking the blue dye.

11. Further still, there is an exceedingly novel and unexpected phenomenon of the claimed invention which occurs between the deposited aerosol mist and the adherent droplets, as shown in FIG. 23; Exhibit E. This figure illustrates the occurrence of a zone of

clearing due to the unexpected curvilinear trajectories of the deposited aerosol mist in close proximity to the droplets. This cleared zone around each droplet further enhances each droplet's isolation from every other droplet, creating a virtual containment zone without the need for any special hydrophobic or electroactive coating of the planar substrate, and without the need for any physical containment between the droplets, such as well walls. This unexpected phenomenon is shown schematically in FIG. 3.ED; Exhibit F. The dynamics of this unexpected phenomenon is shown in FIG. 4.ED; Exhibit G, where the cleared containment zones are clearly visible without the use of wells or a hydrophobic surface coating.

12. I declare that I also am familiar with the cited art in this case. In particular, I understand Henderson et al. to disclose an array comprised of a surface and at least one molecular deposition domain deposited on the surface, in which each domain is 1 micron or less (column 6, line 19 *et seq.*). Additionally, an atomic force microscope (AFM) tip, rather than the applicator pins of the claimed invention, is used by Henderson et al. in a deposition device for depositing the molecular domain onto a substrate.

13. Nowhere do Henderson et al. disclose or suggest an assay system comprising a computer and a set of operating instructions resident in computer software of the computer for operating, a set of reactant dot applicator pins, a separate device for biological sample aerosol mist generation, an xy positioner operatively connected to the dot applicator pins, and a chamber within the device for biological sample aerosol mist generation for control of biological samples, wherein the dots have a diameter ranging from 10 microns to 100 microns and have one or more constituents therein, wherein the aerosolized biological sample mist droplets are applied simultaneously by the separate device for sample aerosol generation without

forming a wetting film, for computer-enhanced assay of any reaction between the sample mist droplets and the constituents, and wherein the dots are not covalently bound to a substrate.

14. Furthermore, contrary to the Examiner's assertions regarding the disclosures of Eipel et al. and Church, it is clear that neither reference teaches nor discloses an aerosol generation device in which a set of reactant dot applicator pins is capable of creating a plurality of reaction spots and a biological sample mist is applied simultaneously by a separate sample aerosol generation device. Rather, Eipel et al. disclose a punch technique for applying a sample and reagents in liquid, not aerosol misted, form (column 4, lines 32-40) and Church solely discloses inkjet deposition in which small drops of liquid, not an aerosol mist, are applied to a support (column 27, line 22).

15. With respect to Engle et al., this reference is cited solely for the purpose of disclosing the use of a printer that is computer-controlled with a set of operating instructions in the computer software. Engle et al. disclose microembossed transparent ink jet receptor films which are suitable for use with desktop ink jet printers for the production of presentation quality overhead transparencies. Engle et al. briefly mention, in the background section, that components of an inkjet system can be grouped into three categories: computer, software, printer; ink; and receptor medium, in which the computer, software and printer will control the size, number and placement of the ink drops. Nowhere do Engle et al. teach or suggest an assay system comprised of two separate computer-controlled devices in which the first computer-controlled device applies reactant dots onto a microarray and the second computer-controlled device generates and applies simultaneously a biological sample aerosol.

16. With respect to Tisone, this reference discloses only a single reagent dispensing apparatus for dispensing atomized chemical reagents onto a membrane in order to

form a diagnostic test strip. Nowhere does Tisone teach or suggest an assay system comprised of a set of reactant dot applicator pins and a separate device for biological sample aerosol mist generation, in which the reactant dot applicator pins deposit reactant dots onto a microarray and the separate device for biological sample aerosol mist generation applies simultaneously a biological sample aerosol mist.

17. With respect to French et al., this reference is cited solely for the purpose of disclosing an aerosol generation device in the form of a nebulizer. French et al. disclose a single apparatus for producing a stream of flowing carrier gas and a stream of small droplets in which the droplets are heated in the carrier gas to produce dry particles that can be analyzed in a suitable analyzer. Nowhere do French et al. teach or suggest an assay system comprised of two separate computer-controlled devices in which the first computer-controlled device applies reactant dots onto a microarray and the second computer-controlled device generates and applies simultaneously a biological sample aerosol.

18. I declare, therefore, based on my understanding of the above-described disclosures, that Henderson et al. do not teach or suggest the claimed invention, and that the disclosures contained in the Eipel et al., Church, Engle et al., Tisone or French et al. references do not cure this deficiency.

19. I declare further that all statements made herein of my own knowledge are true and that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application and any patent issuing thereon.

Scott L. Diamond

Date: 16 Mar 07